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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,936	03/25/2005	Ayrookaran J. Poullose	GC717-2-US	1489

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GENENCOR INTERNATIONAL, INC.
ATTENTION: LEGAL DEPARTMENT
925 PAGE MILL ROAD
PALO ALTO, CA 94304

EXAMINER

MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
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1656

MAIL DATE	DELIVERY MODE
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02/18/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/500,936	Applicant(s) POULOSE, AYROOKARAN J.	
	Examiner WILLIAM W. MOORE	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 15-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 15-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

Applicant's amendments to claims 1, 2, 15, and 16 in the Response filed 9 January 2009 overcome the rejection of record of claims herein under the first paragraph of 35 U.S.C. § 112, which is WITHDRAWN. The amendment of claim 1 introduces, however, a transitional phrase inappropriate for describing an integral molecule that renders the claims herein indefinite and necessitates a new ground of rejection stated below. The amendment of claim 1 to specifically require modification of the GG36 subtilisin amino acid sequence, disclosed to be the amino acid sequence set forth in SEQ ID NO:6, overcomes the rejections of record of claims herein under 35 U.S.C. §§ 102(e) and (f) but necessitates combination of further prior art with the teachings of Estell et al., previously cited, in a new ground of rejection under 35 U.S.C. § 103(a) below.

Claim Objections

Claim 1 is objected to because of the following informalities: Claim 1 erroneously identifies the amino acid sequence with which amino acid position correspondence is to be determined as SEQ ID NO:2, which is the 382-amino acid sequence of the subtilisin BPN' precursor, instead of the 275-amino acid sequence of the mature subtilisin BPN' set forth in **SEQ ID NO:3**. Since the desired identification of "corresponding" amino acids in SEQ ID NO:6 can only be accomplished with reference to SEQ ID NO:3, claim 1 must be amended to state **SEQ ID NO:3** rather than SEQ ID NO:2. Appropriate correction is required in responding to this communication.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

This new ground of rejection is necessitated by Applicant's amendments filed 9 January 2009. Claim 1-3 and 15-18 are rejected as indefinite because claim 1 recites, "consisting essentially of", a transitional phrase format that is ambiguous where claim 1 is actually drawn to a single molecule, an amino acid polymer, wherein each amino acid is covalently bound to at least one other amino acid. Such an integral molecule can have no lesser, physically separate, component thus cannot be distinguished as "consisting essentially of" one component. Such an integral covalently-bound molecule differs from subject matter that can properly be described by the phrase "consisting essentially of", e.g., compositions of matter wherein there are at least two components present and wherein the representation of one component is dominant. Claim 1 is

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construed functionally for purposes of application of the prior art. Appropriate transitional terms for describing the intended polymer are "comprises", "has", and "consists of". The latter term most closely conforms to Applicant's intent to limit the subject matter to the 269-amino acid sequence of SEQ ID NO:6 that is modified by one, or at most two, amino acid substitutions. Claims 2, 3, and 15-18 are included in this rejection because they fail to resolve the ambiguity of claim 1 from which they depend.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3 and 15-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Estell et al., **US 7,332,320**, of record, and Roggen et al., **US 2005/0181446**, made of record herewith.

This new ground of rejection is necessitated by Applicant's amendments filed 9 January 2009. Applicant's arguments at page 4 of the Response filed 9 January 2009 have been fully considered but are moot in view of the new ground of rejection. The amendments to claims 1, 2, and 3 now require that the GG36 subtilisin amino acid sequence, disclose in the specification to be the amino acid sequence set forth in SEQ ID NO:6, be modified by either a V26T or a V26S substitution, a position that is identically numbered in both the amino acid sequences of SEQ IDs NOs:3 and 6, and also by an amino acid substitution N218S which, while this will occur at position 216 in the amino acid sequence of SEQ ID NO:6 the position 216 corresponds to, and is identifiable with reference to, position 218 of SEQ ID NO:3. As discussed in the rejection of record, Estell et al. teach the preparation of subtilisin variants exhibiting altered immunogenic responses, where a subtilisin may be any "naturally-occurring subtilisin" having "amino acid residues at positions that are equivalent to the particular identified residues in *Bacillus amyloliquefaciens* subtilisin" where such a variant produces an altered T-cell response, thus has an altered immunogenicity, because it has one or more amino acid substitutions within a T-cell epitope region that comprises the subtilisin BPN'-correspondent amino acid position 26, which substitution may be "V26S, [or] V26T", and that such variants may also advantageously further comprise one or more stability-conferring amino acid substitutions, including the substitution N218S. Estell et al. further teach the preparation of DNA molecules encoding such variants,

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expression vectors comprising such variant-encoding DNA molecules, host cells comprising such expression vectors, recombinant methods of making such variants utilizing such host cells, and cleaning compositions, including detergent compositions, that comprise such variants. See, e.g., cols 4-10, particularly col. 9 at lines 27-50, the paragraph spanning cols. 9 and 10, col. 10 lines 16-59, the paragraph spanning cols. 11 and 12, the first full paragraph of col. 12, col. 16 at lines 3-5 as well as at line 35, and Example 6 spanning cols. 51 and 52.

Estell et al. do not teach that the amino acid sequence of a particular naturally-occurring *Bacillus lentus* subtilisin should be modified by an amino acid substitution to replace a valine at the subtilisin BPN'-correspondent 26 with a serine or threonine in order to modify that subtilisin's immunogenicity. Thus Roggen et al. are now cited for teaching of the preparation of variants of the naturally-occurring "savinase" subtilisin having the amino acid sequence of their SEQ ID NO:24, which is entirely identical to SEQ ID NO:6 herein, wherein a valine at the subtilisin BPN'-correspondent 26 is replaced by a serine or threonine to provide a variant subtilisin having modified immunogenicity. See, e.g., "savinase" epitope regions "sav4.0", "sav14.0", "sav.16.0", "sav17.0", and "sav18.2" in Table 2 at pages 54-55, as well as claims 76 and 80-85, particularly claim 80. It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a subtilisin variant of claims 1-3 herein by selecting the "savinase" amino acid sequence of SEQ ID NO:24 of Roggen et al. – which is identical to the GG36 subtilisin amino acid sequence of SEQ ID NO:6 herein – to prepare variant subtilisin exhibiting an altered T-cell response, thus an altered immunogenicity, wherein a serine or a threonine is substituted for the valine occurring at position 26, which corresponds to the valine at position 26 of the subtilisin BPN' amino acid sequence of SEQ ID NO:3 herein, wherein the resulting variant will inherently exhibit an improved thermostability. This is because Estell et al. identify a subtilisin BPN'-correspondent region in subtilisins generally that comprises a valine at the subtilisin BPN'-correspondent position 26 and contributes to the generation of a T-cell response in animals and teach that a substitution of serine or threonine to replace the valine in this region will alter the immunogenicity of the variant compared to that of the native subtilisin and because Roggen et al. agree with Estell et al. in particularly identifying the valine at the position 26 in SEQ ID NO:6 herein as contributing to an epitope and teaching, as in their claim 80, that it may be advantageously replaced with a serine or threonine.

It would also have been obvious to one of ordinary skill in the art at the time the invention was made to further introduce the stabilizing N218S substitution according to claims 1-3 herein in such a variant because Estell et al. teach that this is a stabilizing amino acid substitution and

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because such an artisan would readily recognize the asparagine at position 216 in the amino acid sequence of SEQ ID NO:6 as corresponding to the asparagine at position 218 in the amino acid sequence of subtilisin BPN' according to Estell et al. It would further have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the DNA molecule, expression vector, host cell, and cleaning composition of claims 15-18 herein because Estell et al. teach that it is advantageous to make such variant subtilisins by preparing DNA molecules encoding such variants, expression vectors comprising such variant-encoding DNA molecules, and host cells comprising such expression vectors in order to practice a method of making such variants utilizing such host cells and because Estell et al. teach that such variants having altered immunogenicity are advantageously incorporated in cleaning compositions.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. §§ 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Conclusion

No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Jon P. Weber, can be reached at 571.272.0925. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/William W. Moore/
Examiner, Art Unit 1656

/Rebecca E. Prouty/
Primary Examiner,
Art Unit 1652